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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,005	09/11/2000	Erich Wanker	V0179/7001	1379

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Helen C Lockhart
Wolf Greenfield & Sacks
Federal Reserve Plaza
600 Atlantic Avenue
Boston, MA 02210-2211

EXAMINER

GABEL, GAILENE

ART UNIT	PAPER NUMBER
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1641

MAIL DATE	DELIVERY MODE
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12/12/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/485,005	Applicant(s) WANKER ET AL.	
	Examiner Gailene R. Gabel	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 September 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,8-20 and 27-41 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,8-20 and 27-41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/5/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed on September 20, 2007 is acknowledged and has been entered. Claims 5 and 36 have been amended. Currently, claims 1-5, 8-20, and 27-41 are pending and are under examination.

Withdrawn Rejections

2. All rejections not reiterated herein, have been withdrawn
3. In light of Applicant's arguments, the rejection of claims 1, 10, 12, and 18-20 under 35 U.S.C. 103(a) as being unpatentable over Notario et al. (Changes in the membrane proteins of blood cells in the course of embryonal megaloerythropoiesis in relation to hemoglobin maturation) Archivio per le scienze mediche, 135 (1): 1-8 (1978 Jan-Mar) Abstract) in view of Mueller (US Patent 4,094,775) or Gokcen (US Patent 6,428,785), is hereby, withdrawn.
4. In light of Applicant's arguments, the rejection of claims 2-5, 8, 9, 11, 17, and 27-30 under 35 U.S.C. 103(a) as being unpatentable over Notario et al. (Archivio per le scienze mediche, 135 (1): 1-8 (1978 Jan-Mar) Abstract) in view of Mueller (US Patent 4,094,775) or Gokcen (US Patent 6,428,785), as applied to claims 1, 10, 12, and 18-20 above, and in further view of Kalchman et al. (WO 97/18825), is hereby, withdrawn.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-5, 8-20, and 27-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a method of detecting detergent- or urea- insoluble amyloid-like fibrils or amyloid protein aggregates using cellulose acetate or nitrocellulose filters having a pore size capable of retaining detergent- or urea- insoluble amyloid-like fibrils or amyloid protein aggregates, does not reasonably provide enablement for a method of detecting detergent- or urea- insoluble amyloid-like fibrils or amyloid protein aggregates using any given cellulose acetate membrane or nitrocellulose filters. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As set forth in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working

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examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

As to the filter used in the method of detecting the presence of detergent- or urea-insoluble amyloid-like fibrils or amyloid protein aggregates which occur as polyglutamine repeats in the pathological range, the direction and guidance in the specification is notably limited to cellulose acetate or nitrocellulose filters having a specific pore size capable of retaining these high molecular weight detergent- or urea- insoluble amyloid-like fibrils or amyloid protein aggregates. Page 5, first full paragraph provides that the filter used in the method of the invention should comprise of a material with low protein absorption such as cellulose acetate and should have a sufficiently small pore size, specifically 0.45 μm and preferably 0.2 μm or smaller. The same consonant teaching of size requirement is set forth in page 19, first full paragraph. Page 11, third full paragraph (under Figure 3) and page 12, third full paragraph (under Figure 6) of the specification also teach use of cellulose acetate and nitrocellulose membranes that are capable of retaining amyloid-like protein aggregates or aggregated huntingtin protein.

The working examples are also limited to cellulose acetate membranes that are capable of retaining amyloid-like protein aggregates or aggregated huntingtin protein in a dot blot filter retardation assay. Example 8 and Example 9 of the specification, provide use of cellulose acetate membranes having a pore size of 0.2 μm and 0.45 μm , respectively. Based on this limited disclosure and direction, one of the skill in the art would not know how to use alternative pore sizes of cellulose acetate membranes and nitrocellulose filters that would be capable of retaining high molecular weight detergent-

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or urea- insoluble amyloid-like fibrils or amyloid protein aggregates, because increased pore sizes would appear to pass the claimed urea- or detergent- treated amyloid-like protein aggregates or aggregated huntingtin protein that occur with disease, into the filtrate rather than retain them in the filter.

Accordingly, claims 1-5, 8-20, and 27-41 are not commensurate in scope with what is deemed to be enabled in the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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6. Claims 1-5, 8-12, 17-20, 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Notario et al. (Changes in the membrane proteins of blood cells in the course of embryonal megaloerythropoiesis in relation to hemoglobin maturation) Archivio per le scienze mediche, 135 (1): 1-8 (1978 Jan-Mar) Abstract) in view of Tanzi et al. (US Patent 6,365,414).

Notario et al. teach contacting a sample material (circulating blood cells) having membrane proteins, with cellulose acetate membrane for determination of hemoglobin electrophoresis patterns and detecting the presence of large proteins on the cellulose acetate membrane, after solubilization by urea or detergent, sodium dodecyl sulphate (SDS) (see Abstract).

Notario et al. is silent in teaching that the cellulose acetate membrane functions as a filter.

Tanzi et al. disclose an in vitro system for determining formation of A β amyloid which occurs in A β amyloidotic disorders such as Alzheimer's disease. Alzheimer's disease is known to be associated with multiple polyglutamine expansions (see Abstract). Specifically, Tanzi et al. teach filtering a biological sample which contains A β amyloid fibrils on cellulose acetate membrane or nitrocellulose filters (see column 8, lines 18-33 and column 9, lines 31-37 and lines 54-61). Amyloid fibrils are retained on the filter and stained with amyloid staining dye such as Congo Red so as to be detected using electron microscopy (see column 9, line 66 to column 10, line 28 and lines 50-56). Tanzi et al. specifically teach the importance of using a filter having appropriate

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pore size that retains amyloid fibrils and aggregates thereof by preventing their passage through the filter and allows passage of solubilized amyloid peptides (see column 11, lines 48-63).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to have used the cellulose acetate membranes having pore sizes capable of retaining amyloid fibrils and/or amyloid aggregated proteins as used in the method of Tanzi, as a filter capable of capturing and retaining protein aggregates that are insoluble to urea or detergent as in the method of Notario because Notario taught that nitrocellulose membranes have inherent capacity to capture large sized protein molecules from biological samples including those subjected to urea- or detergent- treatment for solubilization, and Tanzi specifically provided that cellulose acetate membranes are conventional and advantageously known for their capability to separate, capture, and isolate so as to filter large amyloid fibrils and aggregated proteins.

Response to Arguments

7. Applicant's arguments filed on September 20, 2007 have been fully considered but are moot in light of the new grounds of rejection.
8. No claims are allowed.
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571)

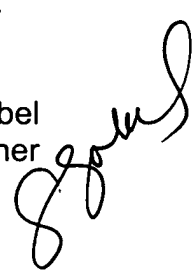
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272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 8:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gailene R. Gabel
Primary Examiner
Art Unit 1641



November 28, 2007